Lung volume reduction surgery for native lung hyperinflation following single-lung transplantation for emphysema: which patients?†

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Abstract

OBJECTIVES: Lung transplantation is an established treatment for patients with advanced emphysema. Double-lung transplantation is favoured to avoid complications following single-lung transplantation, including native lung hyperinflation. Nonetheless, single-lung transplantation continues due to limited donor organ availability. The aim of this study was to evaluate the pre-operative assessment, surgical techniques and outcomes in patients undergoing lung volume reduction surgery for native lung hyperinflation.

METHODS: Eight patients underwent lung volume reduction surgery for native lung hyperinflation between October 2008 and April 2011. Symptoms, pre-operative evaluation, peri-operative morbidity, length of stay, pulmonary function and survival were examined. The mean follow-up was 17 months.

RESULTS: Participants underwent high resolution CT and bronchoscopy with transbronchial biopsy and bronchial washings to exclude alternative causes for deterioration in pulmonary function tests. V/Q scan was performed to assess the contribution of each lung to overall function. Measurement of inspiratory airflow resistance in each lung was performed in one case. Seven patients underwent multiple wedge resections and one underwent bilobectomy. All patients survived to hospital discharge, and mean length of stay was 13.9 days. Functional improvement was demonstrated in all cases at follow-up, with a mean percentage increase of 29.3% in forced expiratory volume in one second and 21.6% in forced vital capacity. Symptomatic improvement was also reported by all patients post-operatively.

CONCLUSIONS: Lung volume reduction surgery for native lung hyperinflation is an effective treatment strategy with an acceptable level of surgical risk. Patient selection, however, remains vital. The non-anatomical multiple wedge excision technique used here was as effective as anatomical lung volume reduction surgery used in other series. With regard to pre-operative assessment, the measurement of single-lung inspiratory airflow resistance is of particular interest. We feel that this may provide an additional method of differentiating between native lung hyperinflation and obliterative bronchiolitis prior to surgery, thus improving patient selection.

Keywords: Transplantation • Hyperinflation • Lung volume reduction

BACKGROUND

Lung transplantation is a well-established treatment for patients with advanced emphysema. The most recently published data from the International Society for Heart and Lung Transplantation Registry reports that chronic obstructive pulmonary disease (COPD) is now the most common indication worldwide for both single- and double-lung transplantations [1]. Double-lung transplantation is still favoured to avoid the complications that can follow single-lung transplantation (SLTx), including native lung hyperinflation (NLH). Nonetheless, due to the issues surrounding donor organ availability, SLTx is likely to continue to be performed in reasonable numbers.

NLH is a unique complication following SLTx for emphysema and contributes to increased morbidity and mortality in this group. The phenomenon can occur acutely, leading to haemodynamic instability and respiratory dysfunction, or may occur as a late complication. In the chronic setting, progressive hyperinflation of the native lung can cause mediastinal shift and compression, resulting in graft dysfunction. It is this chronic picture that is the focus of our study.

There is a substantial body of evidence demonstrating that lung volume reduction surgery is an effective strategy in selected patients with advanced COPD, improving both pulmonary function and quality of life [2–4]. Given this, it would be logical to hypothesize that this treatment could also benefit patients with...
In the past, any surgical intervention following lung transplantation had been avoided due to concerns regarding impaired wound healing and immunosuppressive regimes. In recent years, however, a number of centres have published their experience of post-lung transplant pulmonary resections and have demonstrated the feasibility of surgery within this group [5–8].

In spite of these encouraging reports, lung volume reduction surgery within this patient group is not without risk. The most common causes of mortality in post-transplantation patients are bronchiolitis obliterans (BO) and infective complications [5–8]. In view of this, patient selection and pre-operative work-up are vital in excluding these pathologies, thus improving post-operative outcomes. The aim of this study was, therefore, to evaluate the pre-operative assessment, surgical techniques and outcomes in patients undergoing lung volume reduction surgery for NLH in our institution.

**METHODS**

A review of the thoracic surgical database identified eight patients who had undergone lung volume reduction surgery for NLH within our institution between October 2008 and April 2011. Two further patients with NLH were referred during this period but did not undergo LVRS. NLH was defined as a reduction in clinical function, measured by a decrease in forced expiratory volume in one second (FEV1), accompanied by radiographic evidence of graft compression (Fig. 1). The average age at the time of lung volume reduction surgery ranged from 50 to 69 years with an equal proportion of male and female patients. The average time from initial transplant to lung volume reduction surgery was 49 months (range: 9–120). All patients underwent SLTx for emphysema using standard technique between February 1999 and July 2009. During this time period, 142 lung transplants were performed to treat emphysema, 48 of which were single. Retrospective analysis of the clinical records was performed to provide data regarding symptoms, pre-operative evaluation, surgical procedure and post-operative course.

All eight patients presented with increasing shortness of breath and were found to have deterioration in pulmonary function tests when compared with their early post-transplant performance (Table 1). Subsequent pre-operative assessment included high-resolution computed tomography (HRCT) chest, bronchoscopy and bronchial biopsy to identify NLH and to exclude alternative causes for this decrease in pulmonary function. In addition, V/Q scans were performed in all cases to assess the contribution of each lung to overall function and to identify any particularly poor areas within the native lung. Of note, one patient underwent measurement of inspiratory air flow resistance in each lung as part of the pre-operative evaluation. This was performed during diagnostic bronchoscopy under general anaesthesia; a double-lumen endo-bronchial tube was used to enable lung isolation and the inspiratory air flow resistance of each lung measured by post-inflation occlusion [9]. The rationale behind this assessment is that a raised inspiratory resistance in the native lung when compared with the transplanted lung supports a diagnosis of NLH alone. An increased resistance in both lungs, however, would suggest the coexistence of obliterative bronchiolitis. In this case, the airway resistance in the native lung (10.57 cmH2O/l/s) was markedly raised when compared with the transplanted lung (1.55 cmH2O/l/s), supporting the diagnosis of NLH alone.

Information regarding surgical technique was collected from operative notes and divided into anatomical and non-anatomical resections. The early end-points assessed were length of hospital stay, peri-operative morbidity and 30-day survival. To look at more long-term outcomes, pulmonary function was assessed 6 and 12 months post-operatively and 1 year survival data was collected where possible. Mean follow-up within the group was 17 months.

**RESULTS**

All lung volume reduction surgery was carried out by a single surgeon. Multiple wedge resection with synthetic buttressed staples was performed in seven cases, either via open (four cases) or video-assisted minimally invasive technique (three cases). Only one patient within the group underwent anatomical resection performed using bilobectomy. This was carried out because the severity of the underlying bullous disease prevented the use of standard lung volume reduction procedures. No
patients died within the peri-operative period and the average length of hospital stay was 13.9 days (range: 7–23). There were a number of post-operative complications. Two patients required non-invasive respiratory support for a period of 24–48 h following surgery. Two were treated with antibiotics for respiratory infections, one of whom also developed atrial fibrillation, and a further patient returned to theatre on post-operative day 1 for bleeding. Thirty-day survival for this patient group was 100%. Average length of follow-up was 17 months (range: 4–48). Six patients had a follow-up period of over 12 months and within this group five patients were alive at this time. One patient was readmitted 3 months after the surgery and died because of respiratory failure secondary to pneumonia. Radiological improvement in both NLH and allograft volume was seen in all patients (Fig. 2). Pulmonary function tests were performed at 6 months, 12 months and maximum follow-up (Table 2). These values were then compared with pre-operative baseline values. All patients demonstrated an improvement in FEV₁ with a mean increase of 29.3%. Seven of the eight patients also had an increase in FVC with an overall mean improvement of 21.6%. In addition, all patients reported an improvement in clinical symptoms, exercise tolerance and quality of life; however, objective measurement of this was not documented. Case-specific demographics and outcomes are summarized in Table 3.

**DISCUSSION**

COPD has become the most common indication for SLTx worldwide [1]. Progressive hyperinflation of the native lung is a unique complication seen within this patient group. The result of this is deterioration in pulmonary function caused by compression of the transplanted lung. For this reason, the principal benefit of LVRS in these patients is achieved by improving ventilation of the transplanted lung, and subsequently the overall respiratory function. Pulmonary resections in lung transplant patients were previously thought to carry an excessively high risk due to a combination of immunosuppressive regimes and the extensive disease of the native lung. There is now, however, a significant body of evidence demonstrating the feasibility of LVRS after SLTx [5–8, 10].

<table>
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<th>Patient</th>
<th>Pre-op FEV₁ (l/s)</th>
<th>FEV₁ 3 months (l/s)</th>
<th>FEV₁ 6 months (l/s)</th>
<th>FEV₁ 12 months (l/s)</th>
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One of the largest series was published by Brett Reece et al. [5] in 2008. They reported outcomes for 10 patients who underwent anatomical resections (lobectomy or segmentectomy) for NLH with a mean follow-up of 21 months. Results showed an improvement in function in 87.5% of patients with a peri-operative mortality of 20%. From this, the authors concluded that, despite high risk, lung resection can be undertaken following lung transplant surgery with acceptable mortality and chance for success [5]. The results of the present study further validate this conclusion and have gone on to show both improved survival and post-operative lung function. One area of disparity between the papers, however, is the choice of surgical technique. Brett Reece et al. advocate anatomical resections due to concerns regarding previous outcomes in patients undergoing wedge resection. All but one of our patients underwent traditional LVRS with multiple wedge technique, and no problems with pulmonary healing or prolonged airleak were encountered. This may, in part, be due to the use of staples that have been reinforced with a synthetic buttress to reduce post-operative airleak.

By far, the most common cause of mortality and morbidity in this patient group is BO and other associated infective aetiologies [5–8]. In view of this, the pre-operative evaluation of patients is vital to exclude those with deterioration in lung function caused by these other pathologies. Here we report the use of single-lung inspiratory airflow resistance measurement in one...
case, as part of the pre-operative assessment. Work looking at this technique has suggested that the total inspiratory airflow resistance is much higher in obliterative bronchiolitis than in NLH [11]. Therefore, measurement of the inspiratory resistance of the transplanted lung and native lung individually may provide a further tool for differentiating between the two aetiologies prior to surgery.

A number of other investigations were used in the pre-operative work-up that provide further criteria for patient selection. All patients underwent HRCT chest. We advocate that this must not only show radiological evidence of NLH, but also demonstrate atelectasis and compression of the transplanted lung. If there is NLH alone, then the patient is unlikely to gain significant improvement following LVRS. A ventilation-perfusion scan (V/Q) is also an essential factor in decision-making. The native lung must have a minimal contribution to the overall function. In addition, it must be possible anatomically to remove parts of the native lung with no or little function. Two patients were referred during the study period who did not undergo surgery. In both cases, V/Q scan demonstrated significant contribution of the native lung to overall function. Finally, although basic spirometry is used to demonstrate an objective deterioration in respiratory function, values are not used as an indicator for patient selection.

During the study period, a total of 142 lung transplants were performed in the management of COPD, consisting of 48 single versus 94 double procedures. These findings are encouraging given that double-lung transplantation offers a better functional outcome and avoids complications of the single method, such as NLH. The number of double-lung transplants also increased over the observation period, whereas the single-lung transplants remained relatively stable. These figures would suggest that donor organ availability remains a factor in the surgical options available and that SLTx is likely to continue to be performed in significant numbers.

We acknowledge that the present series has a number of limitations. The size of the patient group within the study is small but is in keeping with previous reports; this is most likely due to the infrequent intervention in this condition. Follow-up in two of the cases unfortunately fell short of the 12-month mark, as it was limited by the time elapsed since surgery. This is, however, an area that can be developed by revisiting the subject in the future to allow us to establish more long-term outcomes. Finally, although our initial work looking at single-lung inspiratory airflow has shown promise in measuring resistance in the native versus transplanted lung, further research is needed to validate this new technique.

Despite these limitations, our data have demonstrated an improvement in function in all patients undergoing lung volume reduction surgery following SLTx, though in some cases this was only a small percentage. These outcomes have been achieved with minimal morbidity and no peri-operative mortality. This study supports previous evidence for the efficacy and feasibility of lung volume reduction surgery in this patient cohort. One reason for these encouraging outcomes may be the strategies used in patient selection and pre-operative evaluation. Therefore, in the setting of careful patient selection, we feel that lung volume reduction surgery for NLH can infer improvements in pulmonary function and clinical symptoms with acceptable surgical risk.

Conflict of interest: none declared.

REFERENCES


